Eli Lilly and Company	LY2245461
Mechanism of Action	Selective estrogen receptor modulator (SERM) http://www.ncbi.nlm.nih.gov/gene/2099; http://www.ncbi.nlm.nih.gov/gene/2100
Overview	LY2245461 is a potent binder to ERa (Ki 0.2 nM) and ERb (Ki 0.4 nM), with potent antagonism of MCF-7 breast cancer cell proliferation in vitro (IC_{50} 0.2 nM). LY2245461 is a SERM, producing estrogen-like agonist activity in reducing vasomotor symptoms in an animal model of hot flashes, while producing minimal estrogen-like stimulation of uterine or mammary tissue.
Safety/Tolerability	LY2245461 has a weak interaction with hERG (IC_{50} > 1 mM). Non-clinical toxicology data supports dosing in humans for up to 4 weeks in duration.
Additional Information	In Ishikawa adenocarcinoma cells, LY2245461 is a potent antagonist (IC_{50} 8.1 nM) with minimal agonist properties (< 4% stimulation compared to tamoxifen, a partial uterine agonist). In vivo LY2245461 is a potent antagonist of estrogen action on the uterus in an immature rat model (ED_{50} 0.05 mg/kg). The compound also displays minimal agonism in a 4 day ovariectomized (OVX) rat model where eosinophil peroxidase activity or uterine wet weight measurements indicate minimal uterine stimulation. In the morphine withdrawal model a pre-clinical model for hot flashes LY2245461 attenuates the naloxone-induced increase in tail skin temperature with an ED_{50} of 0.16 mg/kg. LY2245461 increased hot flashes in postmenopausal women contrary to pre-clinical studies but otherwise was well tolerated.
Suitable for and Exclusions	LY2245461 must not be administered to pre-menopausal or menopausal women and in particular pregnant or lactating women. It has not been evaluated for use in pregnancy, and reproductive toxicity is a possible adverse effect of its use.
Clinical Trials	https://www.clinicaltrialsregister.eu/ctr-search/search?query=eudract_number:2008-001372-75
Publications	None